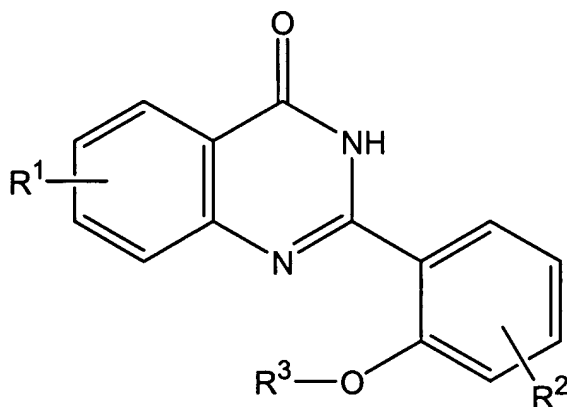


Amendments to the Claims

Please amend the claims to read as follows:

1-49. (Canceled)

50. (Currently Amended) A method of localizing a substantially water-insoluble drug within a solid tumor in an animal, the method comprising administering a water-soluble prodrug to the animal, wherein the prodrug comprises the drug substituted with a prosthetic group that is cleavable by an enzyme that is present in the extracellular space of the tumor and that is produced naturally by cells of the tumor, whereby cleavage of the prosthetic group from the prodrug yields the substantially water-insoluble drug, wherein the prodrug has the structure



wherein

each of R¹ is selected from the group consisting of a hydrogen radical, a radionuclide, a molecule labeled with one or more radionuclides, a boron atom, a molecule labeled with one or more boron atoms, and a boron cage;

R² is ~~independently~~ selected from the group consisting of a hydrogen radical, a radionuclide, and a boron cage;

at least one of R¹ and R² is not a hydrogen radical; and

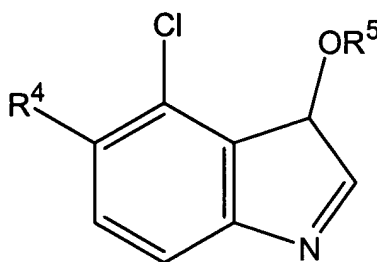
R³ is a prosthetic group that can be cleaved from the prodrug by the enzyme.

51. (Previously Presented) The method of claim 50, wherein R¹ is a hydrogen radical and R² is a radionuclide.

52. (Previously Presented) The method of claim 50, wherein R^1 is a radionuclide and R^2 is a hydrogen radical.

53. (Previously Presented) The method of claim 50, wherein R^3 is a phosphate moiety.

54. (Currently Amended) A method of localizing a substantially water-insoluble drug within a solid tumor in an animal, the method comprising administering a water-soluble prodrug to the animal, wherein the prodrug comprises the drug substituted with a prosthetic group that is cleavable by an enzyme that is present in the extracellular space of the tumor and that is produced naturally by cells of the tumor, whereby cleavage of the prosthetic group from the prodrug yields the substantially water-insoluble drug, wherein the prodrug has the structure



wherein

R^4 is selected from the group consisting of a radionuclide, a molecule labeled with one or more radionuclides, a boron atom, a molecule labeled with one or more boron atoms, and a boron cage, and

R^5 is a prosthetic group that can be cleaved from the prodrug by the enzyme.

55. (Withdrawn) The method of claim 54, wherein R^4 is a radionuclide and R^5 is a beta-D-galactosyl moiety.

56. (Withdrawn) The method of claim 50, wherein R^3 is a sulfate moiety.

57. (Withdrawn) The method of claim 50, wherein R^3 is a peptide moiety.

58. (Withdrawn) The method of claim 50, wherein R^3 is a sugar moiety.

59. (New) The method of claim 50, wherein the enzyme is present in the extracellular space of the tumor at concentrations higher than in the extracellular space of normal tissues.
60. (New) The method of claim 50, wherein the enzyme is selected from the group consisting of an acetylglucosaminidase, an acetylneuraminidase, an aldolase, an amidotransferase, an arabinopyranosidase, a carboxykinase, a cellulase, a deaminase, a decarboxylase, a dehydratase, a dehydrogenase, a DNase, an endonuclease, an epimerase, an esterase, an exonuclease, a fucosidase, a galactosidase, a glucokinase, a glucosidase, a glutaminase, a glutathionase, a glucuronidase, a guanidinobenzoatase, a hexokinase, an iduronidase, a kinase, a lactase, a mannosidase, a nitrophenylphosphatase, a peptidase, a peroxidase, a phosphatase, a phosphotransferase, a protease, an RNase, a reductase, a sulfatase, a telomerase, a transaminase, a transcarbamylase, a transferase, a xylosidase, a uricase, and a urokinase.
61. (New) The method of claim 50, wherein the prodrug is either injected by a route selected from the group consisting of intravenously, intra-arterially, subcutaneously, into the lymphatic circulation, intraperitoneally, intrathecally, intratumorally, and intravesically, or is given orally.
62. (New) The method of claim 50, wherein the drug comprises a radionuclide.
63. (New) The method of claim 62, wherein the radionuclide is selected from the group consisting of a gamma emitting radionuclide, a positron emitting radionuclide, an alpha particle emitting radionuclide, and a beta particle emitting radionuclide.
64. (New and Withdrawn) The method of claim 63, wherein the radionuclide is an alpha particle emitting radionuclide selected from the group consisting of astatine-211, bismuth-212, and bismuth-213.
65. (New and Withdrawn) The method of claim 64, wherein the beta particle emitting radionuclide emits beta particles whose energies are greater than 1 keV.

66. (New and Withdrawn) The method of claim 63, wherein the beta particle emitting radionuclide is iodine-131, copper-67, samarium-153, gold-198, palladium-109, rhenium-186, rhenium-188, dysprosium-165, strontium-89, phosphorous-32, phosphorous-33, or yttrium-90.
67. (New) The method of claim 50, wherein the drug comprises a boron cage.
68. (New) The method of claim 50, wherein the prosthetic group is a phosphate group.
69. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is a sulfate group.
70. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is a glycoside.
71. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is a monosaccharide.
72. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is a polysaccharide.
73. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is an aromatic moiety.
74. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is an amino acid moiety.
75. (New and Withdrawn) The method of claim 50, wherein the prosthetic group is a polypeptide.
76. (New) The method of claim 54, wherein the enzyme is present in the extracellular space of the tumor at concentrations higher than in the extracellular space of normal tissues.
77. (New) The method of claim 54, wherein the enzyme is selected from the group consisting of an acetylglucosaminidase, an acetylneuraminidase, an aldolase, an amidotransferase, an arabinopyranosidase, a carboxykinase, a cellulase, a deaminase, a decarboxylase, a dehydratase,

a dehydrogenase, a DNase, an endonuclease, an epimerase, an esterase, an exonuclease, a fucosidase, a galactosidase, a glucokinase, a glucosidase, a glutaminase, a glutathionase, a glucuronidase, a guanidinobenzoate, a hexokinase, an iduronidase, a kinase, a lactase, a mannosidase, a nitrophenylphosphatase, a peptidase, a peroxidase, a phosphatase, a phosphotransferase, a protease, an RNase, a reductase, a sulfatase, a telomerase, a transaminase, a transcarbamylase, a transferase, a xylosidase, a uricase, and a urokinase.

78. (New) The method of claim 54, wherein the prodrug is either injected by a route selected from the group consisting of intravenously, intra-arterially, subcutaneously, into the lymphatic circulation, intraperitoneally, intrathecally, intratumorally, and intravesically, or is given orally.

79. (New) The method of claim 54, wherein the drug comprises a radionuclide.

80. (New) The method of claim 79, wherein the radionuclide is selected from the group consisting of a gamma emitting radionuclide, a positron emitting radionuclide, an alpha particle emitting radionuclide, and a beta particle emitting radionuclide.

81. (New and Withdrawn) The method of claim 80, wherein the radionuclide is an alpha particle emitting radionuclide selected from the group consisting of astatine-211, bismuth-212, and bismuth-213.

82. (New and Withdrawn) The method of claim 81, wherein the beta particle emitting radionuclide emits beta particles whose energies are greater than 1 keV.

83. (New and Withdrawn) The method of claim 80, wherein the beta particle emitting radionuclide is iodine-131, copper-67, samarium-153, gold-198, palladium-109, rhenium-186, rhenium-188, dysprosium-165, strontium-89, phosphorous-32, phosphorous-33, or yttrium-90.

84. (New) The method of claim 54, wherein the drug comprises a boron cage.

85. (New) The method of claim 54, wherein the prosthetic group is a phosphate group.

86. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is a sulfate group.
87. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is a glycoside.
88. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is a monosaccharide.
89. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is a polysaccharide.
90. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is an aromatic moiety.
91. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is an amino acid moiety.
92. (New and Withdrawn) The method of claim 54, wherein the prosthetic group is a polypeptide.